

Appl. No. 10/089,058
Response dated October 27, 2005
Reply to Office action of June 28, 2005

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Withdrawn) A purified and isolated nucleic acid molecule comprising (a) a nucleotide sequence encoding an A chain of a ricin-like toxin, (b) a nucleotide sequence encoding a B chain of a ricin-like toxin and (c) a nucleotide sequence encoding a heterologous linker amino acid sequence linking the A and B chains, the heterologous linker sequence containing a cleavage recognition site for a specific protease.
2. (Withdrawn) A nucleic acid molecule of claim 1 wherein the specific protease is an MMP or UPA.
3. (Withdrawn) A nucleic acid molecule according to claim 1 wherein the protease is associated with a cancer cell.
4. (Withdrawn) A nucleic acid molecule according to claim 3 wherein the cancer cell is one found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate, cancer or non small cell lung cancer.
5. (Withdrawn) A nucleic acid molecule according to claim 1 wherein the protease is associated with an inflammatory cell.
6. (Withdrawn) A nucleic acid molecule according to claim 5 wherein the cell is one found in rheumatoid arthritis, atherosclerotic cells, Crohn's disease, or central nervous system disease.
7. (Withdrawn) A nucleic acid molecule of claim 1 wherein the A chain is ricin A chain, abrin toxin A chain, diphtheria toxin A chain, Domain III of Pseudomonas exotoxin, volkensin toxin A chain, cholera toxin A chain, modeccin toxin A chain, viscumin toxin A chain or shiga toxin A chain.
8. (Withdrawn) A nucleic acid molecule of claim 1 wherein the B chain is ricin B chain, abrin toxin B chain, diphtheria toxin B chain, Domain I/II of Pseudomonas exotoxin, volkensin toxin B chain, cholera toxin B chain, modeccin toxin B chain, viscumin toxin B chain or shiga toxin B chain.
9. (Withdrawn) A nucleic acid molecule according to claim 1 having a nucleic acid sequence selected from the group consisting of the nucleic acid sequence of pAP301 as shown in Figure 1B (SEQ ID NO:5); the nucleic acid sequence of pAP302 as shown in Figure 2B (SEQ ID NO:12); the nucleic acid sequence of pAP303 as shown in Figure 3B (SEQ ID NO:19); the nucleic acid sequence of pAP304 as shown in Figure 4B (SEQ ID NO:26); the nucleic acid sequence of pAP305 as shown in Figure 5B (SEQ ID

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NO:33); the nucleic acid 5 sequence of pAP308 as shown in Figure 6B (SEQ ID NO:40); the nucleic acid sequence of pAP309 as shown in Figure 7B (SEQ ID NO:47); the nucleic acid sequence of pAP313 as shown in Figure 8B (SEQ ID NO:54); the nucleic acid sequence of pAP314 as shown in Figure 9B (SEQ ID NO:61); the nucleic acid sequence of pAP315 as shown in Figure 10B (SEQ ID NO:68); the nucleic acid sequence of pAP316 as shown in Figure 11B (SEQ ID NO:75); the nucleic acid sequence of pAP318 as shown in Figure 12B (SEQ ID NO:82); the nucleic acid sequence of pAP320 as shown in Figure 13B (SEQ ID NO:89); the nucleic acid sequence of pAP321 as shown in Figure 14B (SEQ ID NO:96); the nucleic acid sequence of pAP322 as shown in Figure 15B (SEQ ID NO:103); the nucleic acid sequence of pAP323 as shown in Figure 16B (SEQ ID NO:110); the nucleic acid sequence of pAP324 as shown in Figure 17B (SEQ ID NO:117); and the nucleic acid sequence of pAP325 as shown in Figure 18B (SEQ ID NO:124).

10. (Withdrawn) A nucleic acid molecule according to claim 1 wherein the nucleotide sequence of the linker is selected from the group consisting of: the nucleic acid sequence of pAP301 as shown in Figure 1A (SEQ ID NO:4); the nucleic acid sequence of pAP302 as shown in Figure 2A (SEQ ID NO:11); the nucleic acid sequence of pAP303 as shown in Figure 3A (SEQ ID NO:18); the nucleic acid sequence of pAP304 as shown in Figure 4A (SEQ ID NO:25); the nucleic acid sequence of pAP305 as shown in Figure 5A (SEQ ID NO:32); the nucleic acid sequence of pAP308 as shown in Figure 6A (SEQ ID NO:39); the nucleic acid sequence of pAP309 as shown in Figure 7A (SEQ ID NO:46); the nucleic acid sequence of pAP313 as shown in Figure 8A (SEQ ID NO:53); the nucleic acid sequence of pAP314 as shown in Figure 9A (SEQ ID NO:60); the nucleic acid sequence of pAP315 as shown in Figure 10A (SEQ ID NO:67); the nucleic acid sequence of pAP316 as shown in Figure 11A (SEQ ID NO:74); the nucleic acid sequence of pAP318 as shown in Figure 12A (SEQ ID NO:81); the nucleic acid sequence of pAP320 as shown in Figure 13A (SEQ ID NO:88); the nucleic acid sequence of pAP321 as shown in Figure 14A (SEQ ID NO:95); the nucleic acid sequence of pAP322 as shown in Figure 15A (SEQ ID NO:102); the nucleic acid sequence of pAP323 as shown in Figure 16A (SEQ ID NO:109); the nucleic acid sequence of pAP324 as shown in Figure 17A (SEQ ID NO:116); and the nucleic acid sequence of pAP325 as shown in Figure 18A (SEQ ID NO:123).

11. (Withdrawn) A plasmid incorporating the nucleic acid molecule of claim 1.

12. (Withdrawn) A baculovirus transfer vector incorporating the nucleic acid molecule according to claim 1.

13. (Currently amended) A recombinant protein comprising an A chain of a ricin-like toxin, a B chain of a ricin-like toxin and a heterologous linker amino acid sequence, linking the A and B chains, wherein the linker sequence contains a cleavage recognition site for a specific protease and is selected from the group consisting of the amino acid sequence of PAP302 as shown in Figure 2C (SEQ ID NO:14); the amino acid sequence of PAP303 as shown in Figure 3C (SEQ ID NO:21); the amino acid sequence of PAP304 as shown in Figure 4C (SEQ ID NO:28); the amino acid sequence of PAP305

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as shown in Figure 5C (SEQ ID NO:35); the amino acid sequence of PAP308 as shown in Figure 6C (SEQ ID NO:42); the amino acid sequence of PAP313 as shown in Figure 8C (SEQ ID NO:56); the amino acid sequence of PAP316 as shown in Figure 11C (SEQ ID NO:77); the amino acid sequence of PAP323 as shown in Figure 16C (SEQ ID NO:112); the amino acid sequence of PAP324 as shown in Figure 17C (SEQ ID NO:119); and the amino acid sequence of PAP325 as shown in Figure 18C (SEQ ID NO:126).

14. (Cancelled).

15. (Previously presented) A protein according to claim 13 wherein the protease is associated with a cancer cell.

16. (Previously presented) A protein according to claim 15 wherein the cancer cell is one found in T- and B cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate, cancer or non small cell lung cancer.

17. (Previously presented) A protein according to claim 13 wherein the protease is associated with an inflammatory cell.

18. (Previously presented) A protein according to claim 17 wherein the cell is one found in rheumatoid arthritis, atherosclerotic cells, Crohn's disease, or central nervous system disease.

19. (Previously presented) A recombinant protein of claim 13 wherein the A chain is ricin A chain, abrin toxin A chain, diphtheria toxin A chain, Domain III of Pseudomonas exotoxin, volkensin toxin A chain, cholera toxin A chain, modeccin toxin A chain, viscumin toxin A chain, or shiga toxin A chain.

20. (Previously presented) A recombinant protein of claim 13 wherein the B chain is ricin B chain, abrin toxin B chain, diphtheria toxin B chain, Domain I/II of Pseudomonas exotoxin, volkensin toxin B chain, cholera toxin B chain, modeccin toxin B chain, viscumin toxin B chain, or shiga toxin B chain.

21. (Cancelled)

22. (Withdrawn) A method of inhibiting or destroying cells having a specific protease comprising the steps of:

(a) preparing a purified and isolated nucleic acid having a nucleotide sequence encoding an A chain of a ricin-like toxin, a B chain of a ricin-like toxin, and a heterologous linker amino acid sequence, linking the A and B chains, wherein the linker sequence contains a cleavage recognition site for the protease;

(b) introducing the nucleic acid into a host cell and expressing the nucleic acid in the host cell to obtain a recombinant protein comprising an A chain of a ricin-like toxin, a B chain of a ricin-like toxin and a linker amino acid sequence;

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(c) suspending the protein in a pharmaceutically acceptable carrier, diluent or excipient, and

(d) contacting the cells with the recombinant protein.

23. (Withdrawn) A method according to claim 22 wherein the protease is an MMP or UPA.

24. (Withdrawn) A method according to claim 22 wherein the protease is associated with a cancer cell.

25. (Withdrawn) A method according to claim 24 wherein the cancer cell is one found in T- and B cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate, cancer or non small cell lung cancer.

26. (Withdrawn) A method according to claim 22 wherein the protease is associated with an inflammatory cell.

27. (Withdrawn) A method according to claim 26 wherein the cell is one found in rheumatoid arthritis, atherosclerotic cells, Crohn's disease, or central nervous system disease.

28. (Withdrawn) A method of inhibiting or destroying cells having a specific protease comprising contacting the cells with an effective amount a recombinant protein according to claim 13.

29. (Withdrawn) A method of treating a cell having a specific protease comprising administering an effective amount of a recombinant protein according to claim 13 to an animal in need thereof.

30. (Withdrawn) A method of treating a cell having a specific protease comprising administering an effective amount of a nucleic acid molecule according to claim 1 to an animal in need thereof.

31. (Withdrawn) A process for preparing a pharmaceutical for treating a cell having a specific protease comprising the steps of :

(a) preparing a purified and isolated nucleic acid having a nucleotide sequence encoding an A chain of a ricin-like toxin, a B chain of a ricin-like toxin, and a heterologous linker amino acid sequence, linking the A and B chains, wherein the linker sequence contains a cleavage recognition site for a specific protease;

(b) introducing the nucleic acid into a host cell and expressing the nucleic acid in the host cell to obtain a recombinant protein comprising an A chain of a ricin-like toxin, a B chain of a ricin-like toxin and a linker amino acid sequence;

(c) suspending the protein in a pharmaceutically acceptable carrier, diluent or excipient.

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32. (Withdrawn) A process according to claim 31 wherein the protease is an MMP or UPA.
33. (Withdrawn) A process according to claim 31 wherein the protease is associated with a cancer cell.
34. (Withdrawn) A process according to claim 33 wherein the cancer cell is one found in T- and B cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate, cancer or non small cell lung cancer.
35. (Withdrawn) A process according to claim 31 wherein the protease is associated with an inflammatory cell.
36. (Withdrawn) A process according to claim 35 wherein the cell is one found in rheumatoid arthritis, atherosclerotic cells, Crohn's disease, or central nervous system disease.
37. (Previously presented) A pharmaceutical composition for treating cancer comprising a recombinant protein of claim 13 and a pharmaceutically acceptable carrier, diluent or excipient.
38. (Previously presented) A pharmaceutical composition for treating inflammation comprising a recombinant protein of claim 13 and a pharmaceutically acceptable carrier, diluent or excipient.
39. (Withdrawn) A pharmaceutical composition for treating a cell having a specific protease comprising a nucleic acid molecule of claim 1 and a pharmaceutically acceptable carrier, diluent or excipient.
40. (Withdrawn) A pharmaceutical composition for treating a cell having a specific protease comprising an amino acid molecule of claim 1 and a pharmaceutically acceptable carrier, diluent or excipient.
41. (Withdrawn) A purified and isolated nucleic acid molecule having a nucleic acid sequence selected from the group consisting of: the nucleic acid sequence of pAP301 as shown in Figure 1A (SEQ ID NO:4); the nucleic acid sequence of pAP302 as shown in Figure 2A (SEQ ID NO:11); the nucleic acid sequence of pAP303 as shown in Figure 3A (SEQ ID NO:18); the nucleic acid sequence of pAP304 as shown in Figure 4A (SEQ ID NO:25); the nucleic acid sequence of pAP305 as shown in Figure 5A (SEQ ID NO:32); the nucleic acid sequence of pAP308 as shown in Figure 6A (SEQ ID NO:39); the nucleic acid sequence of pAP309 as shown in Figure 7A (SEQ ID NO:46); the nucleic acid sequence of pAP313 as shown in Figure 8A (SEQ ID NO:53); the nucleic acid sequence of pAP314 as shown in Figure 9A (SEQ ID NO:60); the nucleic acid sequence of pAP315 as shown in Figure 10A (SEQ ID NO:67); the nucleic acid sequence of pAP316 as shown in Figure 11A (SEQ ID NO:74); the nucleic acid

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sequence of pAP318 as shown in Figure 12A (SEQ ID NO:81); the nucleic acid sequence of pAP320 as shown in Figure 13A (SEQ ID NO:88); the nucleic acid sequence of pAP321 as shown in Figure 14A (SEQ ID NO:95); the nucleic acid sequence of pAP322 as shown in Figure 15A (SEQ ID NO:102); the nucleic acid sequence of pAP323 as shown in Figure 16A (SEQ ID NO:109); the nucleic acid sequence of pAP324 as shown in Figure 17A (SEQ ID NO:116); and the nucleic acid sequence of pAP325 as shown in Figure 18A (SEQ ID NO:123).

42. (Currently amended) A linker protein having an amino acid sequence selected from the group consisting of: ~~the amino acid sequence of PAP301 as shown in Figure 1C (SEQ ID NO:7);~~ the amino acid sequence of PAP302 as shown in Figure 2C (SEQ ID NO:14); the amino acid sequence of PAP303 as shown in Figure 3C (SEQ ID NO:21); the amino acid sequence of PAP304 as shown in Figure 4C (SEQ ID NO:28); the amino acid sequence of PAP305 as shown in Figure 5C (SEQ ID NO:35); the amino acid sequence of PAP308 as shown in Figure 6C (SEQ ID NO:42); the amino acid sequence of PAP313 as shown in Figure 8C (SEQ ID NO:56); ~~the amino acid sequence of PAP309 as shown in Figure 7C (SEQ ID NO:49); the amino acid sequence of PAP313 as shown in Figure 8C (SEQ ID NO:56); the amino acid sequence of PAP314 as shown in Figure 9C (SEQ ID NO:63); the amino acid sequence of PAP315 as shown in Figure 10C (SEQ ID NO:70); the amino acid sequence of PAP316 as shown in Figure 11C (SEQ ID NO:77); the amino acid sequence of PAP318 as shown in Figure 12C (SEQ ID NO:84); the amino acid sequence of PAP320 as shown in Figure 13C (SEQ ID NO:91); the amino acid sequence of PAP321 as shown in Figure 14C (SEQ ID NO:98); the amino acid sequence of PAP322 as shown in Figure 15C (SEQ ID NO:105); the amino acid sequence of PAP323 as shown in Figure 16C (SEQ ID NO:112); the amino acid sequence of PAP324 as shown in Figure 17C (SEQ ID NO:119); and the amino acid sequence of PAP325 as shown in Figure 18C (SEQ ID NO:126).~~

43. (Withdrawn) A nucleic acid molecule according to claim 1 having the nucleic acid sequence of pAP304 as shown in Figure 4B (SEQ ID NO:26).

44. (Withdrawn) A nucleic acid molecule according to claim 1 wherein the linker has the nucleic acid sequence of pAP304 as shown in Figure 4A (SEQ ID NO:25).

45. (Currently amended) A recombinant protein of claim 13 wherein the linker sequence has the amino acid sequence of pAP304 as shown in Figure 4C (SEQ ID NO:28).

46. (Withdrawn) A nucleic acid molecule according to claim 1 wherein (a) comprises a nucleotide sequence encoding a truncated A chain of a ricin-like toxin.

47. (Withdrawn) A nucleic acid molecule according to claim 1 wherein (b) comprises a nucleotide sequence encoding a truncated B chain of a ricin-like toxin.

48. (New) A recombinant protein of claim 13 wherein the linker sequence has the amino acid sequence of PAP313 as shown in Figure 8C (SEQ ID NO:56).